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Prognostic Implication of Nras Gene Mutations in Egyptian Adult Acute Myeloid Leukemia

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Abstract : Background: The pathogenesis of acute myeloid leukemia (AML) involves the cooperation of mutations promoting proliferation/survival and those impairing differentiation. Point mutations of the NRAS gene are the most frequent somatic mutations causing aberrant signal-transduction in acute myeloid leukemia (AML). Aim: The present work was conducted to study the frequency and prognostic significance of NRAS gene mutations (NRASmut) in de novo Egyptian adult AML. Material and methods: Bone marrow specimens from 150 patients with de novo acute myeloid leukemia and controls were analyzed by genomic PCR-SSCP at codons 12, 13 (exon 1), and 61 (exon 2) for NRAS mutations. Results: NRAS gene mutations was found in 19/150 (12.7%) AML cases, represented more frequently in the FAB subtype M4eo (P = 0.028), and at codon 12, 13 (14of 19; 73.7%). Patients with NRASmut had a significant lower peripheral marrow blasts (P = 0.004, P=0.03) and non significant improved clinical outcome than patients without the mutation. Complete remission rate was (63.2% vs 56.5%; p=0.46), resistant disease (15.8% vs 23.6%; p=0.51), three years overall survival (44% vs 42%; P = 0.85) and disease free survival (42.1% vs 38.9%, P = 0.74). Multivariate analysis showed that age was the strongest unfavorable factor for overall survival (relative risk [RR], 1.9; P = .002), followed by cytogenetics (P = .004). FAB types, NRAS mutation, and leukocytosis were less important. Conclusions: NRAS gene mutation frequency and spectrum differ between biologically distinct subtypes of AML but do not significantly influence prognosis and clinical outcome.

Keywords : NRAS Gene, egyptian adult, acute myeloid leukemia, cytogenetics
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